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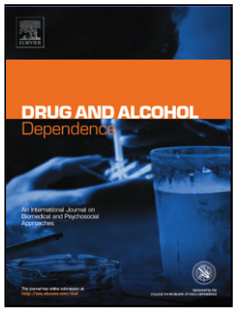

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PII: S0376-8716(14)00919-3
DOI: http://dx.doi.org/doi:10.1016/j.drugalcdep.2014.06.011
Reference: DAD 5188

To appear in: *Drug and Alcohol Dependence*

Received date: 4-4-2014
Revised date: 2-6-2014
Accepted date: 7-6-2014

Please cite this article as: Salom, C.L., Williams, G.M., Najman, J.M., Alati, R.,Does early socio-economic disadvantage predict comorbid alcohol and mental health disorders?, *Drug and Alcohol Dependence* (2014), http://dx.doi.org/10.1016/j.drugalcdep.2014.06.011

Does early socio-economic disadvantage predict comorbid alcohol and mental health disorders?*

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Running title

Socio-economic disadvantage and comorbidity

***** Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:...

ABSTRACT

Background: Alcohol and mental health disorders are highly prevalent in the general population, with co-occurrence recognised as a major public health issue. Socio-economic factors are frequently associated with both disorders but their temporal association is unclear. This paper examines the association between prenatal socio-economic disadvantage and comorbid alcohol and mental health disorders at young adulthood.

Methods: An unselected cohort of women was enrolled during early pregnancy in the large longitudinal Mater-University of Queensland Study of Pregnancy (MUSP), at the Mater Misericordiae Public Hospital in Brisbane, Australia. The mothers and their offspring were followed over a twenty-one year period. Offspring from the MUSP birth cohort who provided full psychiatric information at age 21 and whose mothers provided socioeconomic information at baseline were included (n=2,399). Participants were grouped into no-disorder, mental health disorder only, alcohol disorder only or comorbid alcohol and mental health disorders according to DSM-IV diagnoses at age 21 as assessed by the Composite International Diagnostic Interview. We used multivariate logistic regression analysis to compare associations of disorder group with single measures of prenatal socio-economic disadvantage including family income, parental education and employment, and then created a cumulative scale of socioeconomic disadvantage. **Results**: Greater socio-economic disadvantage was more strongly associated with comorbidity (OR 3.36; CI_{95} 1.37, 8.24) than with single disorders. This relationship was not fully accounted for by maternal mental health, smoking and drinking during pregnancy. **Conclusion**: Multiple domains of socio-economic disadvantage in early life are associated with comorbid alcohol and mental health disorders.

KEYWORDS: Alcohol, comorbid, longitudinal, mental health, socioeconomic

1. INTRODUCTION

Alcohol and mental health disorders are highly prevalent in the general population (Merikangas and Kalaydjian, 2007), with adolescence and early adulthood the prime periods for emergence (Kessler et al., 2005; Teesson et al., 2009). The consequences of these disorders (King et al., 2000; Gore et al., 2011; Mojtabai, 2011; Whiteford et al., 2013), particularly when co-occurring, are increasingly recognised as a major public health issue and their global health and economic burden is high. Mental health and alcohol disorders contribute to 183.9 million Disability Adjusted Life Years annually, peaking in young adults (Whiteford et al., 2013), and treatment of comorbid mental health and alcohol disorders is both more complex (Tiet and Mausbach, 2007; Connolly et al., 2011) and more costly than single disorders (King et al., 2000), with worse projected outcomes (Bruce et al., 2005). As such, understanding how these joint conditions emerge is of great interest to researchers, policy makers and health professionals (Rush and Koegl, 2008; Swendsen et al., 2009; Cerda et al., 2010; Green et al., 2012).

Yet little is known about specific predictors of co-occurrence of these conditions. Beyond individual, familial and hereditary factors, the role of socioeconomic status (SES), long linked to general morbidity (Adler and Stewart, 2010), deserves increased research attention. Cross-sectionally, SES has been associated separately with alcohol disorders (Windle and Davies, 1999; Caldwell et al., 2008; Rush and Koegl, 2008; Swendsen et al., 2009; Adler and Stewart, 2010; Melotti et al., 2011; Young-Wolff et al., 2011; Green et al., 2012; Karriker-Jaffe, 2013) and with depression and anxiety (de Graaf et al., 2002; Gilman et

al., 2003; Melchior et al., 2007; Cerda et al., 2010). A number of studies have linked socio-economic factors and comorbid alcohol and mental health disorders (Ross, 1995; Costello et al., 1997; Windle and Davies, 1999; Armstrong and Costello, 2002; de Graaf et al., 2002; Rush and Koegl, 2008; Cerda et al., 2010; Green et al., 2012; Mulia and Zemore, 2012; Pulkki-Raback et al., 2012), but whether these associations differs from the single disorders is unclear: the use of varying measures makes comparisons challenging (Cerda et al., 2010). Aspects such as low personal income (Ross, 1995; Pulkki-Raback et al., 2012) and lower family social support (Windle and Davies, 1999) have been cross-sectionally associated with comorbid alcohol and mental health problems in large national studies (Mulia and Zemore, 2012). Other studies however have found this to hold only for Caucasian groups (Costello et al., 1997). Similarly, educational status has been implicated in some (Ross, 1995; Green et al., 2012) but not all (Rush and Koegl, 2008) findings.

It is unclear which aspects of SES-based disadvantage are more strongly associated with alcohol and mental health comorbidity. Studies comparing multiple measures of disadvantage have shown increased risk of depression (Eley et al., 2004) for some but not all SES measures used (McLaughlin et al., 2012), but results for comorbidity are again conflicting. Some comparisons have found that low income is more strongly associated than is education (Ross, 1995; Pulkki-Raback et al., 2012), while others suggest that lower education is more strongly associated with common mental disorders (Araya et al., 2003) or comorbid disorders (de Graaf et al., 2002). Generalisation of these seemingly inconsistent associations is complicated by heterogeneity of study designs (Ross, 1995; Costello et al., 1997; de Graaf et al., 2002; Araya et al., 2003; Mulia and Zemore, 2012) and diversity in sample characteristics (Costello et al., 1997; Rush and Koegl, 2008; Green et al., 2012). The cumulative effect of multiple dimensions of socioeconomic disadvantage has been argued

to impact on health problems later in life (Turrell et al., 2003; Marmot, 2005; Chartier et al., 2010; Marie-Mitchell and O'Connor, 2013), but it is unknown whether cumulative disadvantage affects comorbid alcohol and mental health disorders. Some studies have investigated the impact of cumulative adversities on common mental health disorders by using composite measures which allow multiple factors to be considered simultaneously (Eley et al., 2004; Chartier et al., 2010; McLaughlin et al., 2012; Marie-Mitchell and O'Connor, 2013). However, where such composite measures include parental psychopathology, family conflict and health behaviours with socio-economic factors, as for the Adverse Childhood Events scale, it is not possible to distinguish between the impact of SES-based and behavioural factors on the outcome of interest (Marie-Mitchell and O'Connor, 2013). Our study is the first to use a cumulative measure of disadvantage based only on socio-economic factors to investigate its relationship with comorbidity, and considers the effects of parental mental health, drinking and smoking separately.

Another gap in the existing evidence is that most studies have measured SES and comorbidity in adulthood. However, adult SES may be the result of mental health and substance disorders developed during adolescence, which in turn can affect completion of education, and reduce adult employment opportunities and income (Skapinakis et al., 2006; Lee et al., 2013). Some longitudinal studies suggest this may be the case (Costello et al., 1997; Windle and Davies, 1999; Green et al., 2012) as they have shown childhood SES measures to have stronger separate associations with mental disorders and alcohol problems (Laaksonen et al., 2007; Cohen et al., 2010; Green et al., 2012) than measures from later life. No studies have explored more distant SES and its impact on alcohol and mental health comorbidity, yet the fact that childhood measures are more strongly associated with each disorder type points to the possibility that distal socio-economic

disadvantage may be an important factor in the development of alcohol and mental health comorbidity.

Taken together, this evidence suggests the importance of assessing multiple indicators of socio-economic disadvantage in predicting comorbid disorders, and looking at SES very early in life, ideally via a prospective design. This paper aims to examine the impact of a number of indicators of SES from the family of origin, both singly and cumulatively, on comorbid alcohol and mental health disorders in young adults. We use a birth cohort study, the Mater-University of Queensland Study of Pregnancy (MUSP), with detailed information about the parents at the time of pregnancy allowing temporality to be addressed.

2. METHODS

2.1 Study design and participants

The Mater-University of Queensland Study of Pregnancy (MUSP) is a birth cohort study of mothers and children. Mothers were enrolled at their first clinic visit during pregnancy to the Mater Misericordiae Public Hospital in Brisbane between 1981 and 1983, with 7,223 eligible participants at baseline. The MUSP was approved by the Behavioural and Social Sciences Ethics Review Committee at the University of Queensland and has been extensively described elsewhere (Najman et al., 2005). Dyads were followed up at birth, 5 days and 6 months, then 5, 14 and 21 years after birth with 3,778 members of the offspring cohort (52%) participating at age 21. At enrolment and follow-ups, participants gave written, informed consent. Only offspring for whom complete data on prenatal socio-economic factors and mental health and alcohol use at age 21 are available were included in the main analyses.

2.2 Measures

2.2.1 Comorbid mental health and alcohol disorders. At the 21–year follow up, 2,539 offspring participants (35% of baseline) were administered the mental health and substance use disorders modules of the Composite International Diagnostic Interview (CIDI). Responses were coded to yield DSM-IV disorder diagnoses for occurrence over the participant's lifetime, to avoid missing episodes occurring before the year preceding interview. The 'any alcohol use disorder' diagnosis included alcohol abuse and dependence (AUD), whereas 'any mental health disorder' (MHD) included all participants reporting an anxiety, affective, eating or psychotic disorder. Within each of these groups, the presence of multiple disorders was possible.

A four-category variable "Comorbidity Group" was created: No (DSM-IV) disorder; Mental health disorder only (MHD only, i.e., no alcohol disorder); Alcohol use disorder only (AUD only, i.e., no mental health disorder) or Comorbid (i.e., 'any alcohol use disorder' plus 'any mental health disorder'). Concurrence of disorders was examined using ages of onset of most recent episodes for the disorders comprising each individual's comorbid status. All 'Comorbid' participants were found to have episodes of alcohol use disorder and mental health disorder occurring within 12 months of each other, indicating temporal overlap.

2.2.2 Socio-economic measures. SES measures were investigated for association with comorbidity group according to previous findings (Swendsen et al., 2009; Najman et al., 2010; Australian Institute of Health & Welfare, 2012; Pulkki-Raback et al., 2012). Family income, parental employment and parental education were assessed at baseline and coded binomially for disadvantage as below.

Family income was recorded as less than $2600pa, <$5200pa, < $10,400pa, <$15,600pa, <$20,80pa, <$26000pa or >$26000pa. The 1982 minimum wage was $7857; unemployment benefits were $6427 (married) or $3856 (single with dependents) (Cameron,

1983). To account for the number of persons supported by the recorded family income, we conservatively coded un-partnered mothers as disadvantaged if family income was < $5200 and married/de facto participants as disadvantaged if < $10,400.

Maternal pre-pregnancy employment was coded as disadvantaged if recorded as 'unemployed', or 'on benefits'. A small proportion of women who reported 'studying' (0.64%) were also classed as 'disadvantaged', as this was presumed to have limited their employment at that time. 'Home duties' was not coded as disadvantaged as this represented participation in home-based (although unpaid) work. Partner employment was coded as disadvantaged if 'unemployed', 'studying', 'on benefits', 'in prison' or 'no partner'.

Education completed by mother/father was recorded as <Year 10; <Year 12; post-high school qualification or university qualification, and coded as disadvantaged if less than Year 12. Mother's ethnicity was recorded at baseline as white, Asian or Aboriginal/Islander and examined categorically. Children's socio-economic disadvantage at time of CIDI diagnosis (21 years) was estimated using the level of education completed and coded as disadvantaged if less than Year 12. As many (37%) offspring were still studying at that time and 65% living with their parents, their income and employment were not considered measures that would accurately reflect SES-based disadvantage. Although strongly associated with socio-economic disadvantage, we did not separately consider family structure in this study, as this was incorporated in the individual measures of disadvantage described above, and so was highly correlated with these.

2.2.3 Covariates. Maternal age at pregnancy, smoking, drinking, anxiety and depression were included as covariates, as previous studies have shown these to be associated with both mental health and substance use problems in their offspring (Merikangas et al., 1998a;

Alati et al., 2006; Saraceno et al., 2009). Although these items may impact on disorder development during adolescence, baseline measures were used to preclude any potential impact of child disorders. Maternal anxiety and depression were assessed using the Delusions-Symptoms-States Inventory (DSSI; Bedford and Foulds, 1977)). The DSSI contains anxiety and depression subscales; the depression subscale has been found to correlate strongly with other scales of depression, including the Beck's Depression Inventory (Najman et al., 2000), and achieved Cronbach's α values of 0.88 in the maternal sample; the anxiety subscale reached 0.84. Anxiety and depression were recorded as cases if positive for at least four of the seven symptoms from that subscale (Bedford and Foulds, 1977). Maternal smoking (non-smoker/smoker) and binge drinking (never/more than occasionally drank > 5 glasses of alcohol) during pregnancy were self-reported.

Participants' adolescent drinking (Behrendt et al., 2008) and behaviour problems (Ferdinand et al., 2001) have been associated with later alcohol or mental health problems. We used participants' self-reported adolescent drinking (less than 3 drinks/at least 3 drinks per occasion) at age 14. Behavioural problems were also assessed at age 14 using the Achenbach Youth Self Report (Achenbach, 1997). We used the Total Problems scale, with those falling into the higher 10% of the scale scores defined as having behaviour problems, consistent with Achenbach's definition of caseness (Achenbach, 1997).

2.3 Statistical analyses

Each variable was examined individually and correlation analyses undertaken to determine the degree to which overlap may occur. Exploratory factor analysis was undertaken to examine potential variable groupings, using principal-components factoring and varimax rotation. Finally a cumulative scale was constructed where binomial scores

were summed to generate a Socio-Economic Disadvantage Score ranging from 0 to 5. We fitted multinomial logistic regression models with Odds Ratios (OR) and 95% confidence intervals (CI_{95}) to produce point estimates for the relationships between comorbidity group and socio-economic disadvantage, with the No-Disorder group as reference. We initially used individual indicators of SES, then SES factors generated above and finally the composite disadvantage scale. To establish differences between single-disorder groups and the Comorbid group, we reversed the reference category to the Comorbid group and repeated the analyses. In Model 1, we adjusted for potential confounding by maternal age during pregnancy. Since most other influences would likely be on the causal pathway between distal SES and adult comorbidity, we investigated these as potential mediators. In models 2-5, we investigated the roles of maternal mental health, binge drinking and smoking during pregnancy. Factors excluded from the final model included maternal racial background, offspring age and gender, because they were not found to be associated with comorbidity (data not shown). In a supplementary analysis, we compared the impacts of smoking before and during pregnancy on the relationship on the associations reported here. In a second supplementary analysis, we investigated the roles of participants' own drinking and behaviour problems at age 14 and their educational level at age 21 as potential mediators of the effect of distal socio-economic disadvantage.

Finally, we used multiple imputations to assess how loss to follow up may have affected our results. Starting from Missing at Random assumption (Sterne et al., 2009), we used the STATA procedure to multiply impute our missing data (Ware et al., 2012). We used multivariate regression analyses to determine whether our socio-economic variables were associated with attrition, then included these in the imputation process in order to account for the related missingness. Variables used for the imputation models included participant

gender, maternal age, marital status, anxiety, depression, binge drinking and smoking at baseline, which had earlier been found to be associated with loss to follow up (Salom et al., in press), in addition to the prenatal socio-economic disadvantage score and participant education as described above. We used 10 cycles of regression to generate 10 data sets and repeated our final analysis using the imputed data, then repeated with 20 and 50 cycles. All analyses were undertaken using STATA 12.1 (StataCorp, USA).

3. RESULTS

In this sample, 49 % reported no (DSM-IV) disorders; 23% reported a mental health disorder only (i.e. no alcohol disorder); 16% reported an alcohol use disorder only and 12% reported experiencing both mental health and alcohol disorders within a 12 month period (Table 1). Participants in the MHD Only and Comorbid groups had similarly complex mental health disorders (7.3 and 7.5% respectively reported more than 3 diagnoses).

We found weak to moderate correlation between individual SES measures (Supplementary Table 1). Univariate multinomial regressions (Table 2) showed that low family income and maternal employment were associated with comorbidity but not with single disorder groups; low parental education appeared a risk for each disorder group and although effect sizes were largest for comorbidity, these were not distinct from single disorder groups. Paternal employment was not found to be associated with single or dual disorders, and we found no interaction between individual measures of SES.

Principal component analysis showed two factors with eigenvalues of 1.78 and 1.23 respectively. These accounted for 60.24% of the variance: the first loaded most heavily on family income, mother's employment and father's employment (scores 0-3). The second comprised maternal and paternal education (scores 0-2). Factor scores are standardised to a

mean of 0 and standard deviation of 1, which allowed us to compare effect sizes in regression models of comorbidity group (Table 2). Disadvantage based on education (Factor 2) was more strongly associated with comorbidity (OR 1.33; CI_{95} 1.16, 1.52; continuous variable) than that based on economic factors (Factor 1: OR 1.15; CI_{95} 1.00, 1.33).

The composite Socio-Economic Disadvantage scale was associated with the Comorbid group, but not either single-disorder group (Table 2). A distinct dose response was seen; at the highest level of disadvantage, the odds of belonging to the Comorbid group were over three times those for single disorders (Figure 1). Maternal age at baseline was strongly but inversely related to socio-economic disadvantage; as mother's age increased, participants were less likely to be in the most disadvantaged group (OR 0.01; CI_{95} 0.003, 0.01). However there was no difference in the relationships between mother's age and single or comorbid disorders (Supplementary Table 2). Adjusting for maternal age reduced the magnitude of the relationship (Table 3) between socio-economic disadvantage and comorbid disorders but it remained stronger than with single disorder types.

Maternal smoking and binge-drinking in pregnancy, maternal depression and maternal anxiety at baseline were all related to increasing socio-economic disadvantage (Supplementary Table 2a[1]). Separate inclusion of maternal mental health and maternal binge-drinking in pregnancy reduced the magnitude of the disadvantage/comorbidity relationship only slightly and did not remove the difference between comorbid and single disorder relationships (Table 4). Maternal smoking in pregnancy most strongly attenuated the likelihood of comorbidity at all levels of disadvantage, but the relationship of

[1] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:...

comorbidity with greatest disadvantage remained. Maternal mental health, tobacco and alcohol use at other time periods did not change substantively the associations shown in the main analysis (data not shown).

In supplementary analyses, the impact of mothers continuing to smoke during pregnancy was shown to be different to that of smoking before pregnancy (Supplementary Table 3[2]). Although both were associated with comorbidity, pre-pregnant smoking had no impact on its relationship with disadvantage, while smoking during pregnancy accounted for most (but not all) of the relationship. Mother's race was not significantly associated with single or dual disorders. Low education attainment by participants was related to increasing socio-economic disadvantage; their adolescent drinking and behaviour problems were not (Supplementary Table 2b[3]). Adolescent drinking, behaviour problems and low education each attenuated the magnitude of the early socioeconomic disadvantage/comorbidity relationship but both the relationship and the differentiation of comorbidity from single disorder types remained (Supplementary Table 4[4]). Attrition analysis showed that individually, loss to follow up was associated with male gender, lower maternal age, maternal unemployment, and partner unemployment and low education. Maternal anxiety and depression during pregnancy also predicted attrition, as did increasing

[2]Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:...

[3] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:...

[4] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:...

cumulative socio-economic disadvantage score (Supplementary Table 5[5]). Multiple imputation analysis showed very similar results to those from complete case analysis (Supplementary Table 6[6]); sensitivity analyses using 20 and 50 cycles of imputation did not materially change point estimates (results available on request).

4. DISCUSSION

Our study shows for the first time that increasing levels of cumulative prenatal socio-economic disadvantage predict comorbid alcohol and mental health disorders in young adults, with odds ratios three times those for single constituent disorder types. This is not merely reflective of greater disorder *complexity* in the comorbid group; comorbid and mental health only groups had similar proportions of multiple mental health diagnoses. The effect of this gradient is distinct from more proximal SES measures, and appears only partially mediated by factors such as smoking, drinking and/or maternal mental health status during pregnancy. The impact of these factors measured at other time points was not substantively different. Comparison of component dimensions showed that the strongest contributors to the gradient of disadvantage were more likely to be education-based, demonstrating the importance of considering a range of indicators of socio-economic status.

We used multiple measures to assess socio-economic disadvantage derived from family of origin in order to account for the different social processes reflected (Turrell et al., 2003). We explored low family income because it restricts access to material possessions and non-subsidised health services, reduces nutrition and residential stability and so creates

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stress (Skapinakis et al., 2006; Adler and Stewart, 2010). We also investigated parent employment which may limit availability of basic needs and residential security, but also impact on social participation (Ahnquist et al., 2012) and mental well-being not attained when income is derived from benefits (Turrell et al., 2003). Further, parental education may strongly influence health literacy and the potential ability to understand and respond to health challenges, but also impact on personal aspirations, employment opportunities and family income (Australian Institute of Health & Welfare, 2012). Although our study showed some correlation between these measures, each contributed individually to comorbid alcohol and mental health disorders as has been shown for other conditions (Turrell et al., 2003; Chartier et al., 2010; Kawachi et al., 2010).

In line with some cross-sectional studies (de Graaf et al., 2002; Araya et al., 2003), the strongest component of the relationship of SES with comorbidity appears in this study to be education. Other studies found that income was more strongly linked to these outcomes (Ross, 1995; Pulkki-Raback et al., 2012). This may depend on differing education gradients between countries where studies were conducted. Where high school completion rates were very high (70%, e.g., Finland (Pulkki-Raback et al., 2012) and Canada (Ross, 1995)), education played a smaller role than where a steeper gradient was present. In our study, only 30% of the parent sample had completed high school, similar to Dutch (de Graaf et al., 2002) and Chilean (Araya et al., 2003) studies, where strong associations were found between education and comorbidity. As expected, participants' own education reduced the strength of the association between early socio-economic disadvantage and comorbidity

(see Supplementary Table 4[7]). However the association remained with statistical evidence of a difference from single disorder types, demonstrating the unique role of early disadvantage in the development of comorbidity, as opposed to the development of single disorders. Future studies are needed to confirm the robustness of our findings.

The accumulation of prenatal disadvantages showed the strongest association in our study. Those with disadvantage in most areas were at greater risk of developing comorbid disorders, indicating that eliminating disadvantage in one sphere only would be insufficient. For example, in countries where access to health services is not greatly limited by income, this suggests that not only access to material advantages (Bauman et al., 2006) is important, but that factors associated with parental education may affect the family's ability to cope with complex disorders or access the available support or treatment services. This highlights the necessity of considering multiple indicators of disadvantage to allow for contextual differences.

This impact of disadvantage specifically on comorbid disorders is not wholly mediated by parental behaviours, as has been suggested; it appears to also work independently of several factors associated with SES. Maternal anxiety and depression through pregnancy, although regarded as stressors affecting foetal development and later depression and substance use (Merikangas et al., 1998b; Rao, 2010), did not appear to mediate the relationship between disadvantage and comorbidity. Similarly, although persons of higher disadvantage are more likely to be born of mothers who continue to smoke or drink during pregnancy (Guerri et al., 2009; Hannigan et al., 2010), our analyses

[7] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:...

suggest that these covariates did not wholly account for the relationship with comorbidity. The supplementary analysis of maternal smoking appears to indicate an impact during pregnancy which is distinct from that of smoking beforehand. As to the influence of participants' own drinking and behaviour problems in adolescence, a supplementary analysis showed no substantive differences with the results reported here (Supplementary Table 4[8]).

Our findings have several implications. From an epidemiological perspective, they highlight the importance of evaluating the role of socio-economic factors as main effects in the development of substance and mental health disorders, not merely as confounders. The factor comparisons demonstrate the usefulness of multiple measures in the assessment of SES, to allow for variations in population context. The cumulative impact of multiple disadvantages suggests that addressing a single factor (Marmot, 2005; Bauman et al., 2006) will not reduce the likelihood of comorbid disorders in the population. In addition to equalising financial access to medical care (Adler and Stewart, 2010), it may be important to provide other supports to families in order to improve uptake of available interventions. There are also important clinical implications. It will be important for treatment professionals to be aware that those presenting for co-occurring alcohol and mental health disorders are likely to have a history of multiple socio-economic disadvantages. In the context of complex treatment plans required for comorbidity (Tiet and Mausbach, 2007; Connolly et al., 2011), clinicians should consider that as well as having limited financial resources with which to attend services, clients may come from lower education

[8] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:...

backgrounds. As such they will need additional support to understand the disorders and to assist with treatment uptake, plan compliance and management of recurring symptoms.

This paper has significant strengths. It draws on a large and representative community sample, with gradients of income, education and employment allowing comparison of a number of prenatal socioeconomic factors, and is the first of which we are aware to assess the impact of accumulating disadvantage on comorbid alcohol and mental health disorders. The use of longitudinal data from participants and families of origin allows temporality of associations to be addressed in a meaningful way, and eliminates confounding by the impact of early mental health and alcohol disorders on participants' own education, employment and income (Kawachi et al., 2010; Lee et al., 2013). We have shown that although correlated with adult disadvantage, prenatal SES differentiated between single and dual disorders.

The results should be seen in the context of some limitations. Firstly, the largely Caucasian population did not allow racial background to be sufficiently addressed as a socio-economic factor. Antenatal socio-economic variables were self-reported; it is possible that parental education was more reliably recorded than income or employment, which may have resulted in weaker associations involving income. It is worth noting that attrition over 21 years has resulted in our final sample comprising approximately one third of the original cohort, which may have introduced bias into our results. If the socio-economic risk factors and comorbid outcomes described here were less prevalent in those missing, our models would over-estimate the association between pre-natal socio-economic disadvantage and comorbid alcohol/mental health disorders at age 21 (Najman et al., 2005). Our analyses showed that attrition was associated with greater socio-economic disadvantage, such that

disadvantage is likely to have been under-represented in our final sample. It is thus likely that the associations here are a conservative estimate of the impact of socio-economic disadvantage on the development of comorbid alcohol and mental health disorders. Our imputation analysis produced virtually the same results as the complete case analysis, suggesting confidence in the robustness of our findings.

In conclusion, we found that accumulated prenatal socio-economic disadvantage was strongly associated with the development of comorbid alcohol and mental health disorders in young adults, not wholly mediated by maternal health behaviours, and the impact was greater than for single disorders alone.

FIGURE LEGEND

Figure 1. Association of increasing socio-economic disadvantage with comorbid alcohol and mental health disorders, adjusted for maternal age during pregnancy

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Author disclosures

Role of funding source

This work was supported by the National Health and Medical Research Council (NHMRC grant #1009460). R.A. is funded by a NHMRC Career Development Award Level 2 in Population Health (APP1012485). C.L.S is in receipt of an Australian Postgraduate Award. The NHMRC played no further role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Contributors

Authors Najman, Williams and Alati are Primary Investigators for the project which generated these data. Authors Salom, Alati and Williams designed the study; author Salom managed the review of prior literature. Author Salom wrote the protocol, undertook the statistical analysis and wrote the first draft of the manuscript. All authors contributed to conceptual discussions and have approved the final manuscript.

Conflict of interest

All authors declare there is no conflict of interest.

Acknowledgements

The authors thank the MUSP team, the Mater Misericordiae Hospital, and the Schools of Social Science, Population Health and Medicine (The University of Queensland).

Table 1: Participant characteristics at 21 year follow up

Factor	Stage	Category	N (%)
Participants	21 years	Completed CIDI	2539
Gender	21 years	Female	1299 (51.2%)
Age	21 years	Mean ±SD	20.6 years ± 0.86
Comorbidity group	21 years	No disorder	1237 (48.7%)
		MHD	592 (23.3%)
		AUD	406 (16.0%)
		Comorbid	305 (12.0%)
Own education	21 years	< Year 12	514 (20.5%)
Drinking at 14	14 years	Yes	155 (6.4%)
YSR Total problems	14 years	Highest 10% score	172 (8.5%)
Family income	pregnancy	Low	720 (29.8%)
Low maternal education	pregnancy	< Year 12	1791 (71.0%)
Low partner education	pregnancy	< Year 12	1693 (66.7%)
Maternal unemployment	pregnancy	Disadvantaged	312 (12.4%)
Partner unemployment	pregnancy	Disadvantaged	266 (10.6%)
Marital status	pregnancy	Un-partnered	248 (9.8%)
Maternal age	pregnancy	Mean age ±SD	25.0 years ±5.1
Maternal drinking	pregnancy	Yes	128 (5.1%)
Maternal smoking	pregnancy	Yes	914 (36.3%)
Maternal depression	pregnancy	Yes	90 (3.4%)
Maternal anxiety	pregnancy	Yes	247 (10.4%)

Table 2: Univariate models of comorbidity class in young adults, predicted by indicators of pre-natal socio-economic disadvantage (SED)

Disadvantage Measure	Category	MH only OR (CI_{95})	AUD only OR (CI_{95})	Comorbid OR (CI_{95})
Low family income	Yes	1.22 (0.98, 1.52)	0.99 (0.76, 1.28)	**1.32** (1.01, 1.75)
Low maternal education	Yes	**1.31** (1.06, 1.63)	**1.39** (1.08, 1.80)	**1.66** (1.24, 2.23)
Low partner education	Yes	**1.42** (1.15, 1.75)	**1.27** (1.00, 1.61)	**1.64** (1.24, 2.17)
Maternal unemployment	Yes	1.31 (0.98, 1.76)	1.02 (0.71, 1.46)	**1.56** (1.09, 2.22)
Partner unemployment	Yes	0.94 (0.68, 1.31)	1.09 (0.76, 1.57)	1.25 (0.85, 1.84)
SED Factor 1 (disadvantage from parental income & employment)	continuous	1.07 (0.96, 1.20)	1.00 (0.87, 1.14)	**1.15** (1.00, 1.33)
	0	Reference		
	1	1.25 (0.99, 1.60)	0.96 (0.72, 1.28)	1.19 (0.87, 1.63)
	2	1.28 (0.90, 1.80)	1.11 (0.74, 1.66)	**1.58** (1.05, 2.39)
	3	1.26 (0.87, 1.82)	1.30 (0.87, 1.95)	1.51 (0.97, 2.35)
SED Factor 2 (disadvantage from parental education)	continuous	**1.19** (1.08, 1.31)	**1.16** (1.03, 1.30)	**1.33** (1.16, 1.52)
	0	Reference		
	1	1.07 (0.79, 1.47)	1.18 (0.82, 1.68)	**1.65** (1.05, 2.59)
	2	**1.52** (1.15, 2.02)	**1.51** (1.09, 2.10)	**2.34** (1.55, 3.54)
SED scale (5-variable composite score)	0=low	Reference		
	1	1.26 (0.88, 1.81)	1.26 (0.84, 1.90)	1.69 (0.99, 2.87)
	2	**1.46** (1.04, 2.05)	1.41 (0.96, 2.07)	**2.12** (1.29, 3.48)
	3	**1.89** (1.29, 2.77)	1.54 (0.99, 2.39)	**3.02** (1.79, 5.17)
	4	**1.92** (1.02, 3.07)	1.58 (0.91, 2.73)	**2.36** (1.22, 4.59)
	5=high	**1.15** (0.48, 2.73)	0.99 (0.35, 2.78)	**3.97#** (1.65, 9.55)

# denotes that $OR_{(comorbid)}$ is significantly greater (P <0.025) than either $OR_{(MH)}$ or $OR_{(AUD)}$

Table 3: Multinomial model of comorbidity group at age 21, with socio-economic disadvantage as predictor

Socio-economic disadvantage score	Comorbidity group	Unadjusted OR (CI_{95})	Model 1: Maternal age OR (CI_{95})	Model 2: Maternal age, marital status
0		Reference		
1	MH only	1.26 (0.88, 1.81)	1.23 (0.86, 1.78)	1.23 (0.86, 1.78)
	AUD only	1.26 (0.84, 1.90)	1.22 (0.81, 1.84)	1.22 (0.81, 1.84)
	Comorbid	1.69 (0.99, 2.87)	1.64 (0.97, 2.79)	1.64 (0.97, 2.79)
2	MH only	**1.46** (1.04, 2.05)	**1.42** (1.01, 2.00)	**1.42** (1.01, 2.00)
	AUD only	1.41 (0.96, 2.07)	1.37 (0.93, 2.01)	1.37 (0.93, 2.01)
	Comorbid	**2.12** (1.29, 3.48)	**2.06** (1.25, 3.40)	**2.06** (1.25, 3.40)
3	MH only	**1.89** (1.29, 2.77)	**1.78** (1.21, 2.62)	**1.77** (1.20, 2.61)
	AUD only	1.54 (0.99, 2.39)	**1.42** (0.90, 2.22)	1.38 (0.88, 2.17)
	Comorbid	**3.02** (1.79, 5.17)	**2.82** (1.64, 4.86)	**2.76 (**1.60, 4.77)
4	MH only	**1.92** (1.02, 3.07)	**1.73** (1.07, 2.81)	**1.69** (1.02, 2.80)
	AUD only	1.58 (0.91, 2.73)	1.37 (0.78, 2.41)	1.25 (0.69, 2.23)
	Comorbid	**2.36** (1.22, 4.59)	**2.10** (1.07, 4.13)	1.94 (0.96, 3.92)
5	MH only	1.15 (0.48, 2.73)	1.00 (0.41, 2.40)	0.96 (0.39, 2.37)
	AUD only	0.99 (0.35, 2.78)	0.82 (0.29, 2.32)	0.71 (0.24, 2.10)
	Comorbid	**3.97#** (1.65, 9.55)	**3.36#** (1.37, 8.24)	**2.98#** (1.17, 7.63)

# indicates that $OR_{(comorbid)}$ is significantly higher than either $OR_{(MH)}$ or $OR_{(AUD)}$ (P <0.05)
Model 1: adjusted for mother's age at baseline
Model 2: adjusted for mother's age, marital status at baseline (reference is 'partnered')

Table 4: Examining maternal factors as potential mediators: Multinomial models of comorbidity group at age 21, with socio-economic disadvantage as predictor

Socio-economic disadvantage (score)	Comorbidity group	Model 2: Maternal age/MH OR (CI_{95})	Model 3: Maternal age/drinking OR (CI_{95})	Model 4: Maternal age/smoking OR (CI_{95})	Model 5: Maternal age/ MH/smoke/drink OR (CI65)
0		Reference			
1	MH only	1.27 (0.88, 1.85)	1.24 (0.86, 1.79)	1.21 (0.84, 1.75)	1.24 (0.86, 1.81)
	AUD only	1.24 (0.82, 1.89)	1.25 (0.82, 1.89)	1.21 (0.80, 1.82)	1.26 (0.82, 1.92)
	Comorbid	1.70 (0.99, 2.92)	1.61 (0.94, 2.74)	1.58 (0.93, 2.70)	1.59 (0.92, 2.75)
2	MH only	**1.50** (1.06, 2.13)	**1.44** (1.02, 2.03)	1.33 (0.94, 1.87)	1.41 (0.99, 2.01)
	AUD only	1.41 (0.95, 2.09)	1.38 (0.94, 2.04)	1.31 (0.89, 1.93)	1.38 (0.92, 2.06)
	Comorbid	**2.09** (1.25, 3.48)	**1.97** (1.20, 3.26)	**1.78** (1.08, 2.96)	**1.77** (1.05, 2.97)
3	MH only	**1.75** (1.17, 2.62)	**1.80** (1.22, 2.65)	**1.62** (1.10, 2.40)	**1.61** (1.07, 2.41)
	AUD only	1.46 (0.92, 2.32)	1.43 (0.91, 2.25)	1.33 (0.85, 2.09)	1.42 (0.89, 2.26)
	Comorbid	**2.72** (1.55, 4.76)	**2.71** (1.57, 4.67)	**2.36** (1.36, 4.09)	**2.23** (1.26, 3.94)
4	MH only	**1.72** (1.05, 2.84)	**1.75** (1.08, 2.84)	1.48 (0.91, 2.42)	1.52 (0.92, 2.53)
	AUD only	1.48 (0.84, 2.63)	1.39 (0.79, 2.45)	1.24 (0.70, 2.19)	1.41 (0.79, 2.53)
	Comorbid	**2.20** (1.10, 4.37)	1.94 (0.98, 3.84)	1.50 (0.75, 3.00)	1.60 (0.79, 3.24)
5	MH only	1.02 (0.42, 2.49)	0.86 (0.34, 2.15)	0.71 (0.28, 1.79)	0.75 (0.29, 1.90)
	AUD only	0.89 (0.31, 2.55)	0.80 (0.28, 2.28)	0.71 (0.25, 2.03)	0.80 (0.28, 2.32)
	Comorbid	**3.19#** (1.25, 8.12)	**3.10#** (1.26, 7.63)	2.34**¥** (0.94, 5.81)	2.22 (0.86, 5.75)

Model 2: mother's age plus mother's anxiety & depression during pregnancy
Model 3: mother's age plus maternal binge drinking (>5 drinks/session) during pregnancy
Model 4: maternal age plus smoking during pregnancy
Model 5: maternal age, depression, anxiety, smoking and drinking in pregnancy

# indicates that $OR_{(comorbid)}$ is significantly higher than either $OR_{(MH)}$ or $OR_{(AUD)}$ (P <0.05)
¥ indicates that $OR_{(comorbid)}$ is significantly higher than either $OR_{(MH)}$ or $OR_{(AUD)}$ (P <0.08)

Figure 1.